HAWAII BREAST CANCER COALITION
Diagnostic Standards for Early Breast Cancer

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Common Breast Problems

A number of breast conditions exist that may cause a woman concern and provoke a great deal of anxiety. Most of these conditions, however, are not cancer and many in fact need no treatment at all. By doing routine breast self-examinations, a woman will get to know her breasts and know the changes that occur throughout her menstrual cycle. Although most changes in a woman's breast are not cancer, it is important to be evaluated by a health care provider if a change is noticed and to help determine its cause. Changes that should prompt evaluation include a new lump; nipple changes to include persistent scaling, nipple retraction and nipple discharge; new breast pain that seems localized to one particular area of one breast; dimpling of the skin or changes in texture and color of the skin. Any findings on physical examination that are suspicious for cancer should prompt immediate referral to a surgeon regardless of a normal mammogram.

A thorough focused history is important when evaluating a woman with any type of breast abnormality. Important considerations are patient age, pregnancy, a history of prior biopsies, infections, documentation of hormone usage, radiation exposure, a family history of breast cancer, and duration of symptoms. These should be correlated with the physical findings. Important components of the physical examination include examination of the woman in both the upright and supine positon; a thorough systematic examination of the entire breast, nipple-areolar complex, and axillae. It is critically important to make every effort to identify the area of concern to the patient with subsequent documentation. Areas of thickening, nodularity, and lumpiness that are NOT clinically suspicious may be described by the patient as a discrete lump or mass simply because their technical vocabulary is not adequate to describe these changes.

Fibrocystic changes are very common and are related to changes in the circulating levels of estrogen and progesterone. Lumpiness or nodularity with cyst formation are typical and are responsible for the swelling and tenderness that occurs. This is usually most pronounced just before the patient's menses. Wearing a supportive bra (like a running bra), diet alteration, and taking over the counter pain relievers are usually all that are necessary to treat this condition. After menopause, the symptoms related to fibrocystic disease should resolve as should the nodularity. The exception to this is if the patient is taking hormone replacement.

The breast pain that is caused by fluctuating hormone levels will come and go with the patient's menstrual cycle and is usually bilateral. Other conditions not due to hormones can also cause breast pain and include trauma to the breast which may result in bruising, swelling, or a tender lump all of which should resolve after several months. Breast infections seen typically in women who are breastfeeding usually respond to antibiotics and warm compresses. Inflammation of the underlying ribs can also mimic breast pain which is usually worse when taking a deep breath. This usually responds to

motrin or aspirin. Although pain is uncommon as the sole initial symptom of breast cancer, it should not, by itself, exclude the diagnosis of cancer. The pain associated with cancer is less likely to fluctuate, is often confined to one area of one breast, and constant in intensity.

Areas of thickening, nodularity, and lumpiness may occur in a patient's breasts that are not suspicious for cancer. In fact, it is very common for a patient to present to her health care provider because of a "new lump" where the doctor, after a careful physical examination, finds only nodularity or lumpiness without a discrete lump. This is particularly true around the nipple, in the armpit, as well as the inframammary fold where this often feels like a step-off or ridge on examination. It is acceptable to follow a patient through several menstrual cycles and repeat the physical examination. If there is any uncertainty about a vague thickness, nodularity, or lumpiness that is felt, or if the patient has already gone through menopause and has a new dominant lump, asymmetric ill-defined thickening or change in their breast, the patient should be referred to a surgeon for further evaluation and consideration made for biopsy.

Cysts are benign lumps that are filled with fluid. They may be solitary or multiple and involve both breasts. If they become tender, the fluid can be drained from them with a small needle. A fibroadenoma is also a benign lump that is not fluid-filled but is a solid knot of breast tissue. These are usually smooth, rubbery, movable, and can occasionally become tender before a woman's period. Fibroadenomas typically do not go away and are usually removed for diagnosis. In selected cases, these may be observed if they remain stable on follow-up. The diagnosis of a benign fibroadenoma can be made by percutaneous biopsy or by various imaging modalities (mammo and ultrasound). A phyllodes tumor must be considered in the differential diagnosis of a fibroadenoma and addressed accordingly. If a period of observation is selected for management of a fibroadenoma, any change in the characteristics of the lesion (i.e. particularly a rapid increase in size) should prompt immediate biopsy.

Discharge from a woman's nipples may be perfectly normal. In fact, many women can squeeze a small of discharge from one or both nipples. This discharge may be clear, greenish, or milky in appearance. It is more common in women who have given birth. Although the vast majority of women with nipple discharge do not have cancer, any new discharge that is from one breast, from a single duct, and is spontaneous, or is associated with a lump, and is bloody should be evaluated further to help determine its cause. Established discharge that has changed in color or character should also be re-evaluated.

The Dominant Breast Mass:

Although most lumps are benign, particularly in younger women, all new lumps should undergo evaluation by a health care provider experienced in treating breast

diseases. When a lump is found, several things should be considered when addressing it. These include the physical characteristics of the lump, its duration, changes over time, associated pain, and its mammographic appearance. The patient's age, menstrual status, and hormone use; as well as preexisting risk factors for the development of breast cancer are also important considerations. A suspicious lump is one that is irregular, solitary, and discrete from the surrounding breast tissue. It is typically firm or hard, is not freely mobile, and is usually in one breast only. A benign or noncancerous lump on the other hand is one that is typically smooth, soft or firm in consistency; it may be somewhat rubbery and movable, may fluctuate in size, and may be tender to touch. Common causes of benign lumps include fibrocystic changes, cysts, and fibroadenomas.

When should a women with a breast lump be referred to a general surgeon or breast specialist. This will vary with the experience and comfort level of the primary care physician in the management of breast diseases. In general, any patient with a dominant breast mass in which a benign diagnosis is not established should be referred to a surgeon. (Primary care providers should NOT follow any woman with a dominant breast lump). When a breast specialist elects to follow a dominant or discrete lump or mass (i.e. fibroadenoma) three criteria should be met: 1. The lump must have benign characteristics on physical examination 2. The mammogram or ultrasound must be normal or reveal the palpable abnormality. The abnormality must meet the criteria for a benign lesion radiographically 3. A fine needle aspiration (FNA) must be adequate (cellular specimen) and be consistent with a benign diagnosis. If the fine needle aspiration is inadequate or nondiagnostic, or if the clinical experience is limited in interpreting FNA's, then core needle biopsy may be used as an alternative. When all three of these criteria are met (triple test), the lesion can be safely followed with a greater then 98% chance of benignity to be expected. All three criteria must be in concordance with one another. If not, the lesion should be excised.

A patient with a palpable mass suspicious for cancer should have an initial diagnostic mammogram or problem solving imaging evaluation. The purpose of the mammogram is to evaluate the normal surrounding breast tissue and the opposite breast for nonpalpable cancers. It is not to make a diagnosis of the palpable mass. Mammography for a palpable mass should not be performed initially in women less than 30 years. Exceptions to this may include a woman with a clinically *suspicious* mass, strong family history, or biopsy proven breast cancer. Any suspicious mass noted on physical examination requires further evaluation (tissue diagnosis) regardless of a normal mammogram. Likewise, any suspicious mammographic abnormality (BI-RADS 4 or 5) requires tissue diagnosis regardless of a normal physical examination. Ultrasound and aspiration may also be required for a complete evaluation. Most surgeons would prefer that the patient then be referred directly to a surgeon before having a biopsy (with the exception of fine needle aspiration biopsy at the discretion of the PCP). Ultrasound and aspiration may also be required for a complete evaluation. In many instances the work-up is very straightforward. For example, a well-circumscribed, freely moveable nodule in a

young woman’s breast can immediately, safely, and almost painlessly be defined by a simple aspiration.

Management of Mammographic Abnormalities:

A patient with an abnormal mammogram should undergo a clinical breast examination to rule out palpable disease. If there is a suspicious palpable abnormality that corresponds to the mammographic abnormality, this should be managed as per the protocol for the "management of the palpable breast mass". Tissue diagnosis should be obtained and should not generally require localization. Any findings on mammography should be compared to previous mammograms if available. The BI-RADS system is used to characterize mammographic abnormalities; clinical decisions are based upon the probability of malignancy. Additional views may be required to further characterize abnormalities seen on screening CC and MLO views. Magnification and compression views are used to clarify "densities" and "architectural distortions", to rule out confluence of dense breast parenchyma forming a "mass effect", and to characterize the size, shape, density, number, and extent of microcalcifications. Ultrasound is used to differentiate mass lesions seen on mammogram to rule out simple cyst.

American College of Radiology BI-RADS system

BI-RADS 0: Assessment is incomplete, additional radiographic evaluation is needed. Clinical decisions made only after additional imaging is performed

BI-RADS 1: Negative; no further investigation. Routine CBE, MMG, and Counseling.

BI-RADS 2: Benign finding. Routine follow-up recommended as for BI-RADS 1.

BI-RADS 3: Probably benign finding, short f/u interval is suggested (usually at 6 and 12 months) to establish the stability of the mammographic lesion; less then 2% chance of malignancy. Biopsy if any change is noted.

BI-RADS 4: **Suspicious abnormality**, biopsy should be considered

Image guided biopsy - stereotactic or ultrasonographic guided FNA or core biopsy, excisional biopsy, needle localization biopsy. The type of biopsy should be based on a thorough discussion between the patient and the physician. If the biopsy results are negative and the pathologic features correlate with the MMG findings, recommend 6 months f/u MMG. If atypia or malignancy is found, proceed with complete excision or definitive cancer surgery.

BI-RADS 5: Highly suspicious for malignancy, biopsy should be performed. given the high probability of cancer; a benign result short of an excisional biopsy should be interpreted with caution. Surgical biopsy may be necessary to rule out a false negative result obtained by less invasive procedures.

Note: These are guidelines -- management decisions are based on the discussions between the patient and her physician. The patient must be informed of the estimated risk of cancer and the diagnostic options. Factors such as patient's anxiety level, risk factors for breast cancer, and compliance with follow up may influence the course of action.

Indications and Techniques for Biopsy:

A number of techniques are available for cytologic and histologic evaluation of *suspicious* breast abnormalities. The judicious application of a technique appropriate to both the patient and the abnormality is essential. A patient with a single dominant mass in the breast can undergo sampling of the abnormality at the initial evaluation by fine needle aspiration for cytology or core biopsy for histology. In postmenopausal patients, it is advisable to have a recent mammogram to: 1) help in the definition of the palpable abnormality and; 2) to identify occult abnormalities, if any, elsewhere in ipsilateral or the opposite breast. It is preferable to obtain a diagnostic mammogram prior to procuring tissue as a resulting hematoma can obscure the mammographic findings.

Fine needle aspiration for cytology is performed by stabilizing the palpable abnormality with the non-dominant hand and, after creating a small skin weal with local anesthetic, making multiple passes into the abnormality with a 23-or 25-gauge needle attached to a 10 cc. Syringe. With the needle within the substance of the abnormality, note is taken of the "needle-tip sensation" as it is passed back and forth in the thickening or mass with negative pressure applied through the syringe. If fluid is obtained, its color, consistency, and the presence or absence of any blood is noted, as well as whether the palpable abnormality disappears completely or persists in part. When no fluid is obtained, multiple passes are made to aspirate cellular material into the hub of the needle. Negative pressure is then completely discontinued before removing the needle from the breast abnormality. The needle is removed and direct pressure is immediately applied to the aspiration site. A cytologic interpretation regarding the adequacy of the sample should be made immediately. In instances where the sample is not adequate for interpretation, i.e. nondiagnostic (acellular specimen or a paucity of cells), repeat aspiration should be performed at the same setting. Ideally, a cytopathology technician should be present during the procedure. Simple cysts with turbid or greenish fluid, aspiration of which results in disappearance, do not require cytologic evaluation. stereotactic biopsy is not necessary for palpable lesions.

Under some circumstances (failed FNA, increased fibrosis as may be seen in the post-irradiated breast, or particular risk factors), a core needle biopsy may be performed. A 14-gauge hand or spring-activated core biopsy instrument is used to obtain specimens sufficient for histologic examination. A specimen from a core needle is placed in formalin and processed like any other tissue for routine histology. This type of biopsy should be performed by a breast specialist. Incisional biopsies are performed for very large masses; ill-defined lesions (e.g., lobular carcinoma); or other circumstances in which an excisional biopsy would be poorly tolerated or inappropriate. For inflammatory carcinoma, both the breast and the skin should be sampled by incisional biopsy.

Fine needle aspiration and core biopsies can also be obtained for nonpalpable abnormalities under mammographic or ultrasonographic control. Suspicious abnormalities which are nonpalpable AND not amenable to stereotactic biopsy, can be excised in their entirety using wire or dye localization. This procedure is typically performed under local anesthesia with or without the use of IV sedation.

Needle biopsy techniques are not infallible. It may be difficult or impossible to distinguish between cellular atypia and carcinoma, or define important characteristics of a particular tumor. The pathologic interpretation of a breast lesion following FNA or Core Biopsy must be compared to the mammogram and placed into context with the clinical scenario and physical examination. All should be concordant. For example, a negative or benign diagnosis following a stereotactic core biopsy of a BI-RADS 5 abnormality ("cancer until proven otherwise") should raise suspicion. Open biopsy (by needle localization when necessary) may be required.

Evaluation of the High Risk Breast Cancer Patient:

It is now estimated that approximately 5-10% of all new cases of breast cancer is due to a hereditary predisposition. This translates into approximately 18,000 cases per year. Breast cancer that develops in younger women are more likely to have a genetic basis, with current estimates being that 25% of those cases arising in women under the age of 50 and 40% of those arising under the age of 30 have a genetic basis. This makes the identification of these women extremely important since they will be missed in the normal screening process as they become at risk far earlier than when routine mammography is generally started.

Currently, genetic testing of individual women as a routine screening practice is both impractical and potentially harmful. However, it is prudent for each physician to understand the circumstances that place a woman at high risk for breast cancer so that she can be appropriately referred for specialized counseling and care.

Assessing breast cancer risk requires taking a thorough history. Current age, age at

first live birth, age at menarche, number of first degree relatives with breast cancer, and number of prior breast biopsies are all factors in determining risk. However, it is a careful collection of an accurate family history that will help the clinician identify the true "high risk" patient. Hereditary breast cancer is strongly related to a family history of early onset (before age 50) breast cancer, bilateral breast cancers, multiple first degree relatives with breast cancer, and other early onset cancers, especially ovarian cancer.

Women who have families with a history of early onset breast or ovarian cancers, bilateral breast cancer, or multiple first degree relatives with either breast or ovarian cancer have a high likelihood of having a hereditary breast cancer syndrome. To date, the BRCA1, BRCA2, ATM, and TP53 genes have been identified to confer high risk of breast cancer to carrier women. Although the BRCA1 gene has been cloned for genetic testing in the research setting, its routine use in the clinical setting (outside a clinical protocol) is not appropriate. Many medical, psychosocial, and legal uncertainties still exist and are far from being solved.

Women who have been identified as high risk should be referred to a specialist for counseling. Options today include intensive surveillance, participation in chemoprevention studies, and prophylactic surgery. Intense surveillance would include starting annual mammography at least 5-10 years before the youngest case of breast cancer in the family. Chemoprevention studies such as the NSABP and NCI-Milan study have shown some benefit with tamoxifen. Bilateral total mastectomy (subcutaneous mastectomy is not appropriate) may be offered to certain select women.

Women who have families with early-onset breast or ovarian cancer, bilateral breast cancer, or two or more first degree relatives with breast or ovarian cancer should be considered high risk and likely to have a hereditary breast cancer syndrome. Such high risk patients should be referred to an appropriate specialist for counseling and further management. If such specialty care is not available, then the primary care physician should institute early and intense surveillance which would include annual or biannual clinical breast examination in addition to annual mammography at least 5-10 years prior to the earliest onset of breast cancer in the family. If mammography is limited or compromised by extremely dense breast tissue, ultrasonography may play a complimentary role in screening this particular subset of patients. It should be recognized that ultrasonography should not be used as a screening tool for most patients. Its role is as a diagnostic tool to further delineate findings on mammography or physical examination.

Diagnosis and Management of Ductal Carcinoma in Situ (DCIS)

Ductal carcinoma in situ is noninvasive breast cancer, and by definition has no potential

to metastasize. DCIS with microinvasion is invasive breast and should not be confused with pure DCIS; this probably explains why long term survival is not 100% for patients with presumed DCIS treated with mastectomy. 85% of DCIS is discovered by mammogram with the most common mammographic finding being pleomorphic microcalcifications; 10% of mammographically evident DCIS occurs as an uncalcified mass. DCIS that presents as a palpable mass is extremely rare and is almost always associated with a microinvasive component (i.e. invasive breast cancer).

Mammographically detected lesions require an image-directed biopsy. If stereotactic core-needle biopsy is performed, multiple cores (at least 5 samples) should be taken. An X-ray of the specimen should be taken to ensure adequate sampling of microcalcifications. Some microcalcifications or a marker should be left behind to allow future localization for definitive surgery. If a diagnosis of DCIS is made by any percutaneous technique (FNA, core-needle biopsy, mammatomy), open surgical biopsy should be performed since these techniques have a propensity for understaging the lesion. For example, invasive cancer is revealed on open surgical biopsy in up to 20% of DCIS diagnosed by core-needle biopsy. Guided wire open biopsy can be performed for lesions not amenable to stereotactic core-needle biopsy: i.e. a small breast that does not allow full throw of the biopsy device; lesions just under skin; widely dispersed or separated calcifications; uncooperative patient.

The technique is straightforward. The lesion is localize by needle-hook wire, dye injection, or both. This may require multiple wires. Tunneling should be avoided with the incision generally made over the lesion. The specimen should be removed in one piece to allow determination of size and margins. All margins should be inked. The specimen should be sent for permanent, not frozen section. As a general rule, frozen-section of nonpalpable, image-guided biopsy specimens is discouraged. It is difficult to distinguish atypical ductal hyperplasia from DCIS on frozen-section. Additionally, small foci of microinvasion may be lost or rendered uninterpretable by freezing artifact. A frozen-section should be considered only when the information obtained is necessary for immediate therapeutic decisions. Clips should be placed within the biopsy cavity to aid the radiation oncologist. Obtain meticulous hemostasis. Do not close dead space, and avoid the use of drains within the substance of the breast. Radiograph of the specimen is **mandatory**. Postoperative imaging with either mammography or ultrasound should be obtained as soon as the patient can tolerate compression to document complete removal of the mammographic abnormality. Re-excision (or mastectomy if needed) should be performed if residual microcalcifications are found.

Pathologically, margin status is most important feature affecting the risk of local recurrence. A negative margin is obviously preferred. High nuclear grade, necrosis, and comedo pattern are also associated with a higher risk of local recurrence. Micropapillary pattern may be more prone to involvement of multiple quadrants.

Treatment options for DCIS include total mastectomy (axillary dissection is not required)or breast conservation (lumpectomy +/- irradiation). Mastectomy should be performed for multifocal disease (two or more tumors in breast); diffuse, malignant-appearing calcifications; inability to achieve a negative margin following attempts at breast conservation; contraindications to therapeutic radiation (h/o previous XRT to chest or breast; early pregnancy; some collagen vascular diseases). Local excision and radiation therapy is considered standard therapy for patients who are candidates for breast conservation; criteria are similar to those for invasive cancer. Negative margins by at least 1-2 mm is preferred. Occasionally a focally positive microscopic margin may be acceptable. In such cases a radiation boost to the lumpectomy site should be given. A post-excision mammogram should be obtained and should be free of suspicious microcalcifications. Radiation therapy is usually begun as soon as patient has healed adequately, usually 2 to 4 weeks. A whole-breast dose of 4500 to 5000 cGy is typically given. A boost to the primary site, increased to 6000 to 6600 cGy, is an option (particularly in patients with a focally positive margin). Nodal irradiation is not necessary Local excision alone may be considered for very small nonpalpable lesions with favorable histology and negative (this is not considered standard, however).

Regional or systemic recurrence after total mastectomy is 1-2%. (Theoretically this risk should be zero as noted previously. Unfortunately, an unsuspected component of
microinvasion may be present that is overlooked by the pathologist). Local recurrence following lumpectomy and radiation therapy ranges from 4-18%. Most ipsilateral recurrences after breast conserving therapy occur at or near the site of the original lesion. Ipsilateral breast recurrence of both invasive and noninvasive carcinoma after breast conserving therapy is significantly reduced by radiation therapy. Residual, malignant appearing microcalcifications, on a post-mastectomy mammogram, that are not removed prior to radiationis associated with a recurrence rate nearing 100%. Approximately 50% of recurrences after breast conserving therapy and radiation therapy are invasive. Invasive recurrences occur at later intervals than noninvasive ones. Salvage after recurrence (following BCT) – requires mastectomy. Adjuvant therapy using tamoxifen should be considered in the context of a clinical trial.

LCIS (lobular carcinoma in situ; lobular neoplasia):

Lobular Carcinoma in situ is currently thought to be a marker of high risk of subsequent invasive cancer. It confers an equal risk to both breasts with multicentric distribution. If malignancy develops, it is more often ductal cancer, rather than lobular cancer. Development of tumors is not limited to the area of LCIS, but rather random in location LCIS is not detected mammographically but is usually noted as an incidental histologic finding. If LCIS only is found on stereotactic core biopsy, it must be assumed that the target lesion was missed. In this instance, additional evaluation and/or biopsies

should be performed. The incidence of LCIS is 1.0-3.6%. It is found primarily in premenopausal women (suggested by review of biopsy and autopsy specimens), and thought to regress in menopause.

Treatment options are somewhat controversial and range from bilateral simple mastectomy to close observation. Excision of LCIS with negative margins is not necessary. Ipsilateral mastectomy removes all risk of subsequent invasive cancer for that breast, but does not address the equally great risk to the contralateral breast. Bilateral mastectomy is the most aggressive approach and removes all risk for subsequent development of cancer. Advocates of routine contralateral upper outer quadrant biopsy have demonstrated a benefit to only 3% of patients in whom treatment was altered. While recognized that this is too low a yield to recommend for routine screening purposes, two settings in which this may be clinically significant are in women given mantle radiation for Hodgkins disease occurring <30 yrs of age (risk for breast cancer increases ten years post XRT) or in women with BRCA 1 gene mutation. Currently the preferred treatment is observation with close follow-up. (3 of 4 women with LCIS will never develop invasive cancer). In special circumstances (i.e., BRCA 1 or 2 mutation) bilateral mastectomy with or without immediate reconstruction is justified. Tamoxifen should be considered.

Surgical Management of Stage I and II Breast Cancer

Primary treatment of patients with stage I and II invasive breast cancer include: 1. mastectomy with axillary lymph node dissection or; 2. Breast Conserving Therapy (lumpectomy, axillary dissection, and breast irradiation). Six modern, prospective, randomized trials have compared Mastectomy with Breast Conservation Therapy. Although there is heterogeneity between the trials with respect to stage of disease, surgical and radiation treatment, and systemic adjuvant therapy, they have demonstrated that the two treatment options are equivalent. The National Institutes of Health Consensus Development Panel evaluating the appropriate treatment for early stage breast cancer stated in their Consensus Statement in 1992 that “lumpectomy” was the preferred treatment. After a critical review of the world’s literature by representatives of the American Colleges of Radiology, Surgeons, Pathologists, The Society of Surgical Oncology, and the American Cancer Society, a revised consensus statement for standards of care for the diagnosis and management of invasive breast cancer was made and published in CA (1998; 48:83-107). Although mastectomy may be appropriate for some patients, breast conservation followed by radiation therapy remains the preferred treatment in appropriately selected patients with early stage breast cancer. The two basic goals of breast conservation are local disease control and cosmesis. If either are in jeopardy, then mastectomy should be performed.

Absolute Contraindications for Breast Conservation: (Mastectomy should be strongly

considered)

1. First and second trimester pregnancies
2. Multiple primary tumors or multicentric disease
3. Extensive or diffuse indeterminate or malignant microcalcifications
4. A history of therapeutic radiation to the ipsilateral breast region
5. Inability to achieve negative pathologic margins
6. Physical disabilities that preclude the use of radiation therapy

Discussion:

During the first and second trimesters of pregnancy, breast conservation is contraindicated because of the possible teratogenic effects of radiation to the developing fetus. It is possible to perform breast conservation in the third trimester and delay radiation until after delivery. Multiple primary tumors or multicentric disease in different quadrants of the breast are absolute contraindications for breast conservation. This may be manifested by diffuse malignant or indeterminate appearing microcalcifications. Likewise, a history of therapeutic radiation to the ipsilateral breast region (i.e., previous lumpectomy with radiation, mantle radiation for Hodgkin's Disease) is a contraindication for breast conservation as this would result in an excessively high dose of radiation to the region.

Relative Contraindications for Breast Conservation:

1. History of Collagen Vascular Disease
2. Large tumor size
3. Breast Size
4. Tumor Location
5. Geography (logistics and cost)
6. Patient compliance and motivation
7. Patient's preference for mastectomy

Discussion:

In patients with a history of collagen vascular disease (Scleroderma in particular), radiation is tolerated poorly with the possibility of poor wound healing and a poor cosmetic result ensuing. Likewise, in patients with large tumors relative to breast size, adequate cosmesis may be difficult to achieve with lumpectomy. There is recent evidence from the NSABP and M.D. Anderson that preoperative (neoadjuvant therapy) chemotherapy can shrink the primary tumor and thereby enable breast conservation to be performed. This has not resulted in prohibitive local recurrence rates. The location of tumor must be taken into consideration with respect to the choice of local treatment. A

retroarealor tumor may require removal of all, or a part of the nipple-areolar complex. The patient's own breast mound, however, is usually more preferable than a reconstructed breast. A new nipple can be reconstructed at a later date. Large pendulous breasts pose a challenge to the radiation oncologist. Experience is needed to ensure reproductibility of patient set-up and the availability of 6 MeV photon beam radiation. Furthermore, lack of modern radiation facilities and expertise within a reasonable geographic region may make breast conservation therapy not practical in some instances. Patients need to be reliable and willing to return to the hospital on a daily basis while undergoing radiation therapy.

Note:
The presence of the following are NOT contraindications for breast conservation:

- Node Positive Disease
- Presence of breast implants

In the absence of contraindications, radiotherapy should be given as part of breast conservation treatment. Its omission almost always increases the risk of local recurrence. The incidence of local recurrence in the treated breast ranges from 3% to 19%, and is similar to the local failure rate seen after mastectomy. Failures are typically treated with salvage mastectomy. Radiation therapy should be started as soon as possible after surgery and can usually begin 2-4 weeks postoperatively. In patients who are candidates for chemotherapy, radiotherapy is typically given following completion of chemotherapy.

Guidelines for Axillary Dissection in Invasive Breast Cancer

This largely parallels the recommendations of the many organizations contributing to the consensus guidelines recently published by the American Cancer Society in CA - Cancer Journal For Clinicians.

Invasive Breast Cancer

· For patients treated by breast conservation, a separate axillary incision should be used. A transverse or slightly "U"-shaped transverse incision at the lower axillary hair line produces an excellent cosmetic result and good exposure. Surgical treatment of the axilla should involve removal of at least level I and level II nodes. Although isolated involvement of level III nodes is rare, patients with positive nodes have level III involvement over 16% of the time-- level III lymphadenectomy should be considered when multiple nodes are positive.

[Definitions of lymph node levels: Level I nodes: lateral to lateral edge of pectoralis minor. Level II nodes: beneath pectoralis minor muscle; Level III nodes:

medial to medial border of pectoralis minor and lateral to the tendon of the subclavius (Halsted's ligament).]

- The anterior and inferior hemicircumference of the axillary vein should be completely dissected, but, to avoid lymphedema, the posterior area of the vein should be left undisturbed (i.e. do not circumferentially dissect the vein).

- For optimal and accurate staging, 10 or more lymph nodes should be analyzed.

- Lymphedema of the arm occurs both after axillary dissection and axillary irradiation, but incidence of significant edema is low, approximately 5%. When both axillary dissection and axillary irradiation are used, the incidence of this complication becomes much higher, 36% in one series.

- NSABP B-04 suggests that women who have axillary recurrence following an initial treatment regimen which avoids axillary dissection can be successfully salvaged if they have a subsequent axillary recurrence. Evidence that inadequate axillary dissection can compromise survival does exist, however. In a Danish series o 3,128 patients, a higher axillary recurrence and significantly lower survival was seen in those patients with <5 nodes dissected. Initial treatment which avoids treatment of the axilla remains controversial, but has been considered for certain histologies associated with a very low risk of axillary involvement.

- Sentinel node biopsy for breast cancer patients is under active clinical review. Currently in Hawaii this procedure is usually performed with oversight from institutional review boards.

An Alternative Approach to the Axilla: Sentinel Lymph Node Surgery

The presence or absence of lymph node metastases represents the single most important prognostic factor in breast cancer. The presence of regional metastases decreases 5-year survival by up to 40% compared to those patients that have no evidence of nodal metastases. Although the standard surgical approach to treating women with breast cancer has become increasingly more conservative, the management of the axilla continues to be controversial.

Clinical examination of the axilla is not accurate in assessing axillary lymph node metastases. Because of this, axillary sampling is performed to assess the status of the regional nodes. Axillary node dissection, however, remains the most morbid part of the surgical management of breast cancer. The need for general anesthesia, postoperative lymphedema, neuropathy of the arm, seroma formation, formation of painful neuromas, and local wound problems remain significant issues for patients

undergoing axillary dissection. These complications are associated with increased hospitalizations, increased overall costs, and considerable discomfort to the patient.

The rationale for axillary node dissection includes accurate pathologic staging to provide biologic information regarding prognosis, regional control of metastatic disease to the axilla, and to affect the natural history of the disease with a curative intent. Historically, the status of the axillary lymph nodes has also been utilized in planning systemic therapies, enrollment into adjuvant protocols, and to make treatment decisions. Increasing evidence suggests, however, that even low risk individuals with node negative disease can benefit from adjuvant systemic therapies thus raising the issue of the necessity of routine axillary node dissection. The therapeutic value of the procedure has been called into question. Axillary metastases are routinely regarded as indicators of and not governors or instigators of metastatic disease. Regardless of whether or not one believes in the therapeutic efficacy of axillary node dissection, it is clear that the only patients that have the potential to benefit are those with metastatic disease.

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In 1992, Morton and colleagues reported on a novel technique to identify lymph nodes at the highest risk for harboring metastatic disease in regional nodes of patients with cutaneous melanoma. This technique has been termed lymphatic mapping and sentinel node dissection. The sentinel lymph node (SLN) is defined as the first node (or nodes) in the lymphatic basin into which a primary tumor site drains. The initial studies involved the use of a vital blue dye injected around the primary site. The dye is then taken up by the draining lymphatics and regional nodes. The sentinel node(s) initially takes up the dye more avidly then the second or third echelon nodes. This lymph node is then harvested and sent for a focused pathologic evaluation. It has been shown that the histology of the SLN reflects the histology of the remainder of the nodes in the lymphatic basin.

Sentinel lymph node surgery has been extensively studied in melanoma patients with multiple randomized trials showing the efficacy of this minimally invasive technique. It has since been demonstrated to be feasible in patients with breast cancer and is the subject of intense study on a national level. In 1994, Guiliano and coworkers published the initial report of intraoperative lymphatic mapping and sentinel node dissection in patients with invasive breast cancer. Since that initial report, a number of reports have confirmed the utility and efficacy of this technique and have validated the initial hypothesis that when breast cancer metastasizes to the regional lymph nodes, it most frequently goes to the sentinel lymph node. Sensitivity, specificity, and diagnostic accuracy are greater then 90% in large series, with false negative rates typically reported as less then 5%. A general consensus is that a combination of a vital blue dye and a radiotracer are complimentary modalities in identifying and harvesting the sentinel node.

The technique is a multidisciplinary approach that entails a peritumoral injection of radiocolloid and dye, lymphoscintigraphy to map the draining lymphatics, and intraoperative mapping using a hand-held gamma detector with SLN harvesting. The SLN is identified by an increased radioactivity in the node compared to background radioactivity in the axilla. If blue dye also used, the SLN should also be stained blue. The procedure should be performed under an IRB protocol. Patients enrolled should undergo standard axillary sampling as part of the protocol. Proceeding to SLN dissection alone should only be done after appropriate quality control has been established at the institution and an acceptable false negative rate of less than 5% is shown.

In the future, biologic tumor markers and characteristics of the primary tumor may be identified which will accurately predict biologic behavior and determine who needs adjuvant systemic therapy. This will be in lieu of axillary lymph node dissection. Until then, axillary lymph node dissection will continue to remain as part of the standard surgical procedure to obtain staging information on which adjuvant treatment strategies are based. The implications of Sentinel Lymph Node Surgery are then obvious; a minimally invasive procedure that can be done under local anesthesia with minimal morbidity for the patient and that allows for the successful sampling of the axilla providing full nodal staging.

Breast Reconstruction:

Modern breast reconstruction can offer the patient undergoing mastectomy a near normal-appearing breast. The techniques employed are a far cry from those of even a few years ago which at best produce a "breast mound" at the surgical site. Tissue expanders, silicone or saline implants, and autologous vascularized flaps offer a range of options for both the surgeon and patient. With proper pairing of patient and technique the plastic surgeon should be able to offer an oncologically sound, surgically safe and aesthetically acceptable reconstruction to most women.

Patient selection is perhaps the most important factor that determines whether breast reconstruction will be successful or not. Regardless of the surgeon's expertise or technique employed, a poorly selected patient will guarantee frustration. Prior to mastectomy every woman should at least be offered the chance to discuss reconstruction. During this initial consultation the plastic surgeon attempts to properly marry the patient's physical and emotional status, desires and clinical staging with the various reconstructive possibilities. In addition, the surgeon must assure that the woman, after being properly informed of the required surgical steps and potential complications, is committed for the long run. Breast reconstruction often requires several months and multiple procedures to best assure a symmetric, pleasing result. Once informed, the woman's first decision is whether or not to choose reconstruction at all. Some seemingly ideal candidates elect not to undergo reconstruction. This decision should obviously be respected and the patient never pushed. Instead, we simply assure her that delayed reconstruction is always an option should she reconsider.

How does one select immediate versus delayed reconstruction? Put simply, immediate reconstruction offers several advantages over delayed reconstruction and unless specifically contraindicated is usually the best choice. Specific advantages of immediate reconstruction include a generally superior cosmetic result, decreased cost and anesthetic risk compared to two- stage procedures, and preserved positive body image. The only contraindications to immediate reconstruction include an inability to achieve local-regional control and lack of patient desire.

Once immediate reconstruction is chosen the next decision is autologous versus alloplastic material. The time and physiologic investment required, the size and shape of the opposite breast, as well as anatomic constraints and contraindications are the primary determinants of which pathway to take. Either route requires several months before the final result is achieved. Both usually require at least 2 or 3 procedures. Additional minor procedures or touch-ups are frequently required over the next several months regardless of the pathway chosen. Nipple/areolar reconstruction is usually the final finishing touch. It is a simple office-based procedure and is performed between 3 and 6 months postop. Tissue expanders/implant reconstruction is often chosen because it is quicker and physiologically less stressful. It often adds only an hour or so to the mastectomy time.

Hospital stay is not affected. With autologous reconstruction, there is a significant physiologic investment. Three to six hours of operating time is required in addition to the mastectomy. Hospital stay may be increased by up to a week.

The goal of symmetry influences the approach; the size and shape of the opposite breast may present a significant challenge. A woman with a small to moderate size breast and with little or no ptosis may be best served by a tissue expander followed by an implant. In a woman with a larger ptotic breast, however, tissue expanders are unlikely to achieve a symmetric result. Instead, autologous tissue is preferred. The opposite (non-involved) breast may be surgically altered to improve the chance of symmetry. It may be reduced, lifted, or even augmented to help achieve a better match.

Finally several anatomic situations exist which may contraindicate autologous tissue reconstruction. The patient may be very thin with no autologous tissue to spare.Previous abdominal operations may also preclude a TRAM flap. Previous thoracic procedures may preclude a Latissimus flap. Specific examples are discussed in the following section.

Indications, advantages, and complications
(tissue expansion/implant vs autologous tissue)

Tissue expansion with subsequent implant placement is indicated in patients who do not wish to undergo flap reconstruction; thin patients without adequate excess abdominal tissue; patients in whom previous operations have left significant abdominal scarring which precludes flap transfer; and very elderly patients or patients with significant medical problems. The major advantages of tissue expansion and implant reconstruction include the lack of additional scarring, the minimally increased operative requirement, and unaffected hospital stay. Major complications associated with tissue expander/implant placement include device failure, skin necrosis with implant exposure and infection (much increase in irradiated tissue), and long term capsular contracture.

Autologous tissue reconstruction is most commonly performed using a transverse rectus abdominus myocutaneous flap (or TRAM flap). A TRAM flap creates a new breast mound by using the rectus abdominus muscle and overlying skin and fat. The TRAM is ideal for patients who have a larger ptotic opposite breast, some redundant tissue, no previous major abdominal operations and no comorbid conditions. Cigarette smoking, obesity, large abdominal scars, diabetes, autoimmune disease, and severe emotional illness are all associated with higher complication rates. Nonetheless, these are all merely relative contraindications. Every patient must be individually assessed. The only true absolute contraindication to a TRAM flap is a history of a previous abdominoplasty. Such patients may be candidates for other sources of autologous tissue. The complications associated with TRAM flaps range from minor wound problems to abdominal hernias and partial flap loss. Total flap loss while devastating, is quite rare.

Finally, consider a few frequently asked questions.

Is a skin sparing mastectomy oncologically sound ?

When properly performed there is no increased risk of local or distant recurrence in patients with T1 or T2 disease.

Does breast reconstruction adversely affect disease free survival?

The risk of local recurrence and development of a second primary are similar. In reconstructed patients compared with patients undergoing mastectomy alone. Can breast reconstruction be safely performed in patients requiring neoadjument therapy ?

Studies and personal experience have shown that properly selected individuals may undergo either type of reconstruction without difficulty or delay, or without an increased risk of complications. The prudent course, however, is to delay reconstruction.

Are there significant cost advantages to implant based reconstruction?

The initial cost savings of implant reconstruction is lost when corrected for unsuccessful attempts and the cost of additional surgeries are included. Autogenous breast reconstruction alternatives prove most cost effective.

Follow-up After Treatment for Breast Cancer:

All patients who have completed their primary treatment for breast cancer should have regular follow-up surveillance. The frequency of follow-up visits should be adjusted according to individual patient's needs. The following issues and schedule should be considered:

a) The need to discuss and manage early side effects of therapy, plan a follow-up program and provide general support. (This visit is usually scheduled 4 to 6 weeks after therapy.)
b) The need to establish a post-treatment baseline, detect early recurrences and teach breast self-examination. (This visit is usually 4 to 6 months after therapy.)
c) The need for regular physical and mammographic examination to detect potentially curable disease. The National Comprehensive Cancer Network recommends that women who have a lumpectomy for cancer should undergo mammography of the treated breast at six months after surgery and then mammography of both breasts on an annual basis. Women who have a mastectomy should get a diagnostic mammogram of the remaining breast annually after surgery.
d) The need to provide support and counseling may require additional visits for some women, particularly for the first few years.

e) If metastases develop, the frequency of visits must be determined by the symptoms, course of disease and need for further treatment.

- All visits should include a medical history. For women who are taking Tamoxifen, it is important to ask about vaginal bleeding. Physical examination should include both breasts, regional lymph notes, chest wall and abdomen. The arms should be examined for lymphedema. Annual visits should include mammographic examination.
- Routine laboratory and radiographic investigations should *not* be carried out for the purpose of detecting distant metastases.
- Patients should be encouraged to report new, persistent symptoms promptly, without waiting for the next scheduled appointment.
- Breast self-examination should be taught to those women who wish to carry it out.
- Psychosocial support should be encouraged and facilitated.
- Participation in clinical trials should be facilitated and encouraged.
- The responsibility for follow-up care should be formally allocated to a single physician, with the patient participating as much as possible. The patients should always be fully informed of these arrangements.
- Communication between all members of the therapeutic team must be ensured to avoid duplication of visits and tests.
- Patients non-compliant with follow-up should be contacted by phone and/or by registered mail and this should be documented in the medical record.

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